

REMARKS

Claims 19-36 currently appear in this application. The Office Action of February 5, 2003, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Claims 19-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification is said only to enable detection of probes which comprise the pH or potential sensitive fluorophore attached to a steroid, to a head group of a sphingolipid or to the head or a lipid having two 14-carbon chains which interact with a lipid bilayer.

This rejection is respectfully traversed. Claim 19 has been amended to recite that the surface is a lipid-based surface. This term includes lipid bilayers as well as lipid monolayer structures. Support for this amendment can be found in the specification as filed at page 7, lines 24-28, "A lipid conjugated with a pH- or potential-sensitive fluorophore is incorporated into the liposome or other membrane bilayer... The probes may also be incorporated into lipid monolayer structure, such as

stable micelles and emulsion droplets, as well as other lipid phases, such as the cubic phase."

The Examiner has alleged that claims 34 and 35 on the grounds that the fluorophore probe is not structurally delimited in these claims. However, it should be noted that the limitation added in the previous amendment to claim 34 is that the probe must be covalently attached to the polymer surface. The structure of the probe is irrelevant. What is relevant is that it is covalently attached to the polymer surface and, thus, inherently, stably incorporated at the surface. Claim 34 has been amended to emphasize this property.

The Examiner also asserts that the quantity of experimentation in this area is extremely great because of the significant variability of the ability of compounds to be incorporated into surfaces. The Examiner specifically states that, even with regards to the narrower embodiment of lipid bilayers, it would require significant experimentation to identify other stabilizing agents, which could function other than those expressly listed in claim 19.

It is respectfully submitted that applicant is not claiming "stabilizing agents... other than those expressly listed in claim 19". The present invention is limited to those defined in claim 19, with the additional

limitation that the surface to which a probe is incorporated is a lipid-based surface. The probe's modification by "...a steroid, to a head group of a sphingolipid or to a head group of a lipid having at last two chains, each chain comprising at least 14 carbon atoms in length, and wherein each chain is independently selected from the group consisting of acyl, alkyl or alkenyl" is sufficient to achieve the claimed stable incorporation of the modified probe into the lipid-based surface.

In referring to the unpredictability of the art and the state of the prior art, the Examiner asserts that one cannot predict what elements are necessary to stabilize the fluorophore in a position near the surface, and what elements of the fluorophore would function in a surface-independent manner. As indicated above, the amendments to claims 19 and 34 make it clear that the surface has been defined as a lipid-based surface. Those skilled in the art will recognize that the probes, as modified according to claim 19, will be stably incorporated into the lipid-based surface from interaction between the lipids within the surface and the group attached to the probe.

Although working examples are not required for enablement, see, for example, MPEP Section 2164.03 the presence of only one working example should never be the

sole reason for rejecting claims as being broader than the enabling disclosure. However, in the present application three working examples are provide with respect to the first aspect of the invention, the HC-PE probe. Additional examples in the specification showing good results are lissamine, rhodamine-dioleoyl phosphatidyl ethanolamine (LR-PE, see, for example, Figures 7, 8, and 11) and with fluorescein-phosphatidyl ethanolamine (F-PE, as in Figures 9, 14, and 15). Thus, the specification provides working examples with other probes.

With respect to the attached group, it is true that the only group exemplified is phosphatidyl ethanolamine. However, one skilled in the art of lipids will know how to identify and select other "groups" encompassed in the definition provided in claim 19 which can, on the one hand, be attached to a fluorophore and, on the other hand, be incorporated into a lipid based surface.

The present amendment limits the claims to lipid-based surfaces. The "stabilizing" feature of the probe, as defined in claim 19, is sufficient to obtain the desired stable incorporation into lipid-based surfaces, independent of the type of the probe employed.

Claims 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner alleges that claims 34 and 35 encompass a genus of fluorophores which are substantially not altered upon binding or dissociation of the species at the surface.

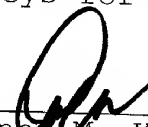
This rejection is respectfully traversed. As this language has been deleted from claim 34, and thus from dependent claim 35, this rejection is now moot.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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